

What is claimed is:

1. A transgenic nonhuman mammal whose germ or somatic cells contain (i) a first heterologous nucleic acid sequence encoding a transcriptional activator whose expression is under the control of a CaMKII α promoter and (ii) a second heterologous nucleic acid sequence encoding a protein whose expression is under the control of a promoter responsive to the transcriptional activator in a regulatable manner.
2. The transgenic nonhuman mammal of claim 1, wherein the transcriptional activator comprises rtTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.
3. The transgenic nonhuman mammal of claim 1, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
4. The transgenic nonhuman mammal of claim 3, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
5. The transgenic nonhuman mammal of claim 3, wherein the expression of the calcineurin inhibitor is induced by doxycycline.
6. The transgenic nonhuman mammal of claim 1, wherein the transcriptional activator comprises tTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.

- 5
7. The transgenic nonhuman mammal of claim 6, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
8. The transgenic nonhuman mammal of claim 7, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
- 10
9. The transgenic nonhuman mammal of claim 7, wherein the expression of the calcineurin inhibitor is repressed by doxycycline.
- 15
10. The transgenic nonhuman mammal of claim 1, wherein the mammal is selected from the group consisting of a mouse, a rat, a sheep, a cow, a dog, a pig, and a primate.
- 20
11. A mammalian cell comprising (i) a heterologous first nucleic acid sequence encoding a transcriptional activator whose expression is under the control of a CaMKII α promoter and (ii) a second heterologous nucleic acid sequence encoding a protein whose expression is under the control of a promoter responsive to the transcriptional activator in a regulatable manner.
- 25
12. The mammalian cell of claim 11, wherein the transcriptional activator comprises rtTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.
- 30

13. The mammalian cell of claim 11, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
- 5 14. The mammalian cell of claim 13, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
- 10 15. The mammalian cell of claim 13, wherein the expression of the calcineurin inhibitor is induced by doxycycline.
- 15 16. The mammalian cell of claim 11, wherein the transcriptional activator comprises tTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.
- 20 17. The mammalian cell of claim 16, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
- 25 18. The mammalian cell of claim 17, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
19. The mammalian cell of claim 17, wherein the expression of the calcineurin inhibitor is repressed by doxycycline.
- 30 20. The mammalian cell of claim 11, wherein the cell is an oocyte, an embryonic stem cell or a neuronal cell.

- 5 21. A composition of matter comprising (i) a first nucleic acid encoding a transcriptional activator whose expression is under the control of a CaMKII α promoter and (ii) a second nucleic acid encoding a protein whose expression is under the control of a promoter responsive to the transcriptional activator in a regulatable manner.
- 10 22. The composition of matter of claim 21, wherein the first and second nucleic acids exist in the same nucleic acid molecule.
- 15 23. The composition of matter of claim 21, wherein the transcriptional activator comprises rtTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.
- 20 24. The composition of matter of claim 21, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
- 25 25. The composition of matter of claim 24, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
- 30 26. The composition of matter of claim 24, wherein the expression of the calcineurin inhibitor is induced by doxycycline.
27. The composition of matter of claim 21, wherein the transcriptional activator comprises tTA and the promoter of the second nucleic acid sequence comprises a tetracycline-responsive sequence.

- 5
28. The composition of matter of claim 27, wherein the protein encoded by the second nucleic acid sequence is a calcineurin inhibitor.
29. The composition of matter of claim 28, wherein the calcineurin inhibitor comprises the carboxy-terminal autoinhibitory sequence of calcineurin.
- 10 30. The composition of matter of claim 28, wherein the expression of the calcineurin inhibitor is repressed by doxycycline.
- 15 31. A method for determining whether an agent inhibits long-term potentiation in a mammal comprising
- (a) administering the agent to the transgenic mammal of claim 5, to which doxycycline has been administered;
 - (b) measuring the resulting long-term potentiation in the mammal; and
 - (c) comparing the long-term potentiation so measured to the long-term potentiation measured in a control transgenic mammal of claim 5 to which doxycycline, but no agent, has been administered, a decrease in long-term potentiation relative to the control mammal indicating that the agent inhibits long-term potentiation in a mammal.
- 25
- 30 32. A method for determining whether an agent inhibits long-term potentiation in a cell comprising
- (a) contacting a cultured hippocampal sample from the brain of the transgenic mammal of claim 5

with the agent, wherein the cells of the sample have been exposed to doxycycline;

(b) measuring the resulting long-term potentiation in the hippocampal sample; and

5 (c) comparing the long-term potentiation so measured to the long-term potentiation measured in a hippocampal sample from a control transgenic mammal of claim 5, wherein the cells of the sample have been exposed to doxycycline, but no agent, a decrease in long-term potentiation relative to the control mammal indicating that the agent inhibits long-term potentiation in a mammal.

10
15 33. A method for determining whether an agent inhibits long-term memory formation, retention or recall in a mammal, which comprises

(a) administering the agent to the transgenic mammal of claim 5, to which doxycycline has been administered;

20 (b) measuring the memory formation, retention, or recall of the mammal in (a) via a behavioral test;

25 (c) comparing the memory formation, retention, or recall so measured to that of a control transgenic mammal of claim 5 to which doxycycline, but no agent, has been administered, a decrease in memory formation, retention, or recall relative to the control mammal indicating that the agent inhibits memory formation, retention, or recall.

30

- 5 34. The method of claim 33, wherein the behavioral test is selected from the group consisting of the Barnes circular maze, the novel object recognition task, an object exploration task, the Morris water maze and the 8-arm radial maze.

2025-11-26 14:26:06